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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894,806	06/28/2001	Alan L. Greener	25436/1712	4116

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/894,806	GREENER ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to a request for continued examination and amendment filed on 2/12/04. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/12/04, has been entered. Claims 81-82 have been cancelled. Claims 1-80 are pending in this action.

Claim Objections

Claims 4, 21, 28 and 60 are objected to because of the following informalities: In claim 4, line 2, a space occurs prior to the word "electroporation buffer", in claim 21, line 2, a space occurs prior to the word "glass-forming matrix", in claim 28, there are two occurrences of the word "is", the first prior to "a polysaccharide" in line 1 and the second prior to "selected from the group" in line 2, in claim 60, line 3, a space occurs prior to "thereof".

Claim 15 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1, upon which claim 15 is dependent states that the cells are dried above freezing while claim 15 states the cells are dried above 0°C.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of generating storage stable E.coli competent cells in which the cells are dried at temperatures greater than freezing in the presence of a glass-forming matrix, does not reasonably provide enablement for a method for generation of storage stable competent cells in which the competent cells are any other prokaryotic or eukaryotic cell in which the cells are dried at temperatures greater than freezing. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) **Nature of invention**. The invention recites a method of generating storage stable cells in which competent cells are dried at temperatures greater than freezing. The cells are not freeze-dried. The method utilizes cell culture techniques.

2) **Scope of the invention**. The base claim is broad in that any competent cell made by any method is considered and the method only requires that the cells are dried at temperatures of greater than freezing. Furthermore, the cells can be stored at temperatures ranging from above -80 °C to above 20°C for at least one month and maintain transformation efficiencies of at least 10^5 transformants/μg DNA.

3) **Number of working examples and guidance**. The specification teaches that a variety of cells, prokaryotic and eukaryotic can be rendered competent for transformation and following competence can be used in the instant method of generating storage stable competent cells (see e.g. page 8, last paragraph). Applicants specifically teach the use of E. coli competent cells that are washed twice in 20% trehalose and then resuspended in 20% trehalose and dried under vacuum at temperatures of 10°C to 30°C (examples 1 and 3) or 30°C (example 6). The specification teaches that trehalose is a preferred saccharide glass-forming matrix (see e.g. page 12, paragraph 2).

These cells maintained 10% viability compared to control cells and were found to be competent following storage at room temperature for 60 days. Control cells and dried cells were made competent by the same methods however, the control cells were frozen at -80 °C but were not dried according to the instant invention. Transformation efficiency was measured and dried cells were found to be between 80% and 168% of control cells (see example 3 and table 1, page 22).

Guidance for the generation of competent cells by a variety of methods is provided and is well known in the art for a variety of cell types (see page 11). The specification further teaches that the cells made competent by any method are contacted with a solution comprising a water-

soluble glass-forming matrix material and a description of these matrices is provided in the specification (see page 12-13). While guidance for the administration of the matrix to E.coli cells is provided, it is not clear from the teachings of the specification how the concentration or type of matrix for a variety of different cell types should be determined.

4) **State of Art**. Methods of making competent cells are well known in the high art. However, the ability to generate "storage stable" competent cells is not a well-developed art.

5) **Unpredictability of the art**. It is unclear how the disclosed method should be altered if cells other than E.coli are used and as the composition of the cells that are being dried at temperatures above freezing differs. Specifically, in the disclosed examples the cells are washed of storage media and then resuspended in just 20% trehalose. Is this step of removing competence buffer and resuspension in glass-forming matrix required of the method? The specification does not address this issue. Nor does it provide a rational as to how the invention works such that one of skill in the art could reliably extrapolate the results seen for E.coli to other types of cells. Therefore, the development of a method for the generation of storage stable competent cells that is applicable to a wide variety of cells by simply drying cells at a temperature greater than freezing is highly unpredictable.

6) **Summary**. The invention recites a methods for the generation of storage stable competent cells. The unpredictability of using the claimed invention with a variety of cells and without glass forming matrix is high and therefore, it is unpredictable that any cell in any competence buffer can be made storage stable upon drying at temperatures above freezing.

In view of predictability of the art to which the invention pertains and the lack of established clinical protocols and the inability to predict for whom the therapies would be

required: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue unpredictable experimentation in order to practice the claimed invention.

Claims 47-77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants claim a genus of compositions comprising competent cells and glass-forming matrix wherein the glass forming matrix is greater than 15 °C.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

The instant specification teaches that competent cells are contacted with a solution comprising water-soluble glass-forming matrix material in which the material is hydrophilic and

comprises a glass transition temperature from 10 °C to 80 °C. Trehalose, sucrose, mezitose, raffinose, maltitol, sorbose, lactitol, dextrose, sugar alcohols, sugar ethers, sugar acids and polysaccharides are disclosed suitable glass forming matrixes. However, none of the glass transition temperatures for these compounds are provided. For purposes of exemplification of the methods, E.coli cells are contacted with 20% trehalose. The disclosure of this single combination is not accompanied by a disclosure as to its glass transition temperature properties. Therefore, there is no clear description of the structural or functional characteristics required of a composition to have a glass transition temperature that meets the requirements of the claims. Neither applicant nor the prior art provide a correlation between the composition of E.coli cells in 20% trehalose. Given the large size and diversity of cell-matrix combinations and the inability to determine which will also have the proper transition temperature, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-14, 25, 27, 30, 46, 60, 62 and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9-14 are vague and indefinite in that the metes and bounds of "said competent cells are stored" are unclear. There are two occurrences of competent cells in independent claim 1, competent cells that have not been dried and competent cells that have been dried. Therefore, it is unclear to which the independent claims are referring.

Claims 25, 27, 30, 60, 62 and 68 are vague and indefinite in that the metes and bounds of the word "derivative" are unclear. It is unclear the nature and number of steps required to obtained a "derivative" of saccharide or polyol. The term implies a number of different steps that may or may not result in a change in the functional characteristics of saccharide or polyol from the source that it is "derived from".

Claim 46 is vague and indefinite in that the metes and bounds of "said cells" are unclear. There are several occurrences of competent cells in reference claims, particularly cells that have not been dried and cells that have been dried. Therefore, it is unclear to which the independent claims are referring.

Conclusion

Claims 1-80 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

March 3, 2004

GERRY LEFFERS
PRIMARY EXAMINER